

B3
Amended

N-Ac-Sar-Gly-Val-D-Ile-Thr-Hser-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-DalloIle-His-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Nva-Ile-Arg-ProNH-n-Butyl,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Nva-Ile-Arg-ProNH-iso-Butyl,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Nva-Ile-Arg-ProNH-iso-Amyl,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Nva-Ile-Arg-ProNH-n-hexyl,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Nva-Ile-Arg-ProNH-(3,3-dimethyl)butyl,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Nva-Ile-Arg-ProNH-(2-ethoxy)ethyl,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Nva-Ile-Arg-ProNH-(2-isopropoxy)ethyl,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Nva-Ile-Arg-ProNH-(3-methoxy)propyl,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Nva-Ile-Arg-ProNH-(cyclopentyl)methyl,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Nva-Ile-Arg-ProNH-cyclohexyl,
N-Ac-Sar-Gly-Val-allo-Ile-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Lys-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Trp-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-3,3-Dipheylala-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-3-Benzothienylala-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-3,4-diF-Phe-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Pen(Bzl)-Thr-Nva-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Leu-Thr-Gln-Ile-Arg-ProNHCH(CH₃)₂,
H-Sar-Gly-Val-D-Leu-Thr-Gln-Ile-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Leu-Thr-Nva-Gln-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Leu-Thr-Nva-Pro-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Leu-Thr-Nva-Ser-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Leu-Thr-Nva-Trp-Arg-ProNHCH₂CH₃,
N-Ac-Sar-Gly-Val-D-Ile-Thr-Nva-Ile-Arg-ProNHCH₂CH₂OH,
N-Ac-Sar-Ser-Val-D-Ile-Thr-Nva-Ile-Arg-ProNHCH₂CH₂OH, and
N-Ac-Sar-Gly-Val-D-Ile-Thr-Leu-Ile-Arg-ProNH((R)-1-cyclohexylethyl).

REMARKS

Claims 1-14, 16, and 18-32 are still pending in the subject application.

The amendment accompanying these remarks amends claim 1 to correct minor typographical errors and makes the corresponding corrections in the Summary of the Invention.

The amendment also adds sixteen additional species to claim 12, support for which is found in the following parts of the specification: Example 19 on page 64, lines 2-11; Example 21 on page 64, lines 25-27 and page 65, lines 1-6; Example 25 on page 66, lines 16-24; Example 39 on page 72, lines 16-24; Example 40 on page 73, lines 2-10; Example 41 on page 73, lines 13-20; Example 100 on page 98, lines 28-31 and page 99, lines 1-3; Example 172 on page 124, lines 27-32 and page 125, lines 1-3; Example 173 on page 125, lines 6-15; Example 104 on page 100, lines 8-16; Example 107 on page 101, lines 9-17; Example 108 on page 101, lines 20-28; Example 109 on page 102, lines 2-10; Example 9 on page 59, lines 2-11; Example 155 on page 118, lines 25-31 and page 119, lines 1-2; and Example 318 on page 173, lines 2-8.

CONCLUSION


Entry of the proposed amendment and allowance of Claims 1-14, 16, and 18-32 is respectfully requested.

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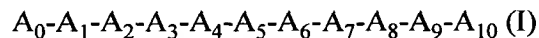
ABBOTT LABORATORIES
Telephone: (847) 937-3810
Facsimile: (847) 938-2623

Respectfully submitted,
J. Henkin, et al.


B. Gregory Donner
Registration No. 34,580
Attorney for Applicants

VERSION OF THE SPECIFICATION WITH MARKINGS
TO SHOW CHANGES MADE

In one aspect, the present invention provides a compound of [the] formula [of]:



or a pharmaceutically acceptable salt, ester, solvate or prodrug thereof, wherein:

A_0 is an acyl group selected from:

- (1) $R-(CH_2)_n-C(O)-$; wherein n is an integer from 0 to 8 and R is selected from hydroxyl; methyl; N-acetylamino; methoxyl; carboxyl; cyclohexyl optionally containing [a] one or two double bonds and optionally substituted with one to three hydroxyl groups; and a 5- or 6-membered [ring] aromatic or nonaromatic ring optionally containing one or two heteroatoms selected from nitrogen, oxygen, and sulfur, wherein the ring is optionally substituted with a moiety selected from alkyl, alkoxy, and halogen;

VERSION OF THE CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

1 (Amended). A compound of the formula:



or a pharmaceutically acceptable salt, ester, solvate or prodrug thereof, wherein:

A_0 is an acyl group selected from:

- (1) $R-(CH_2)_n-C(O)-$; wherein n is an integer from 0 to 8 and R is selected from hydroxyl; methyl; N-acetylamino; methoxyl; carboxyl; cyclohexyl optionally containing [a] one or two double bonds and optionally substituted with one to three hydroxyl groups; and a 5- or 6-membered [ring] aromatic or nonaromatic ring optionally containing one or two heteroatoms selected from nitrogen, oxygen, and sulfur, wherein the ring is optionally substituted with a moiety selected from alkyl, alkoxy, and halogen; and
- (2) $R^1-CH_2CH_2-(OCH_2CH_2O)_p-CH_2-C(O)-$; wherein R^1 is selected from hydrogen, alkyl, and N-acetylamino, and p is an integer from 1 to 8;

A_1 is an amino acyl residue selected from:

- (1) alanyl,
- (2) asparaginylyl,
- (3) citrullyl,
- (4) glutaminylyl,
- (5) glutamyl,
- (6) N-ethylglycyl,
- (7) methionyl,
- (8) N-methylalanyl,
- (9) prolyl,
- (10) pyro-glutamyl,
- (11) sarcosyl,
- (12) seryl,
- (13) threonyl,

- (14) $-\text{HN}-(\text{CH}_2)_q-\text{C}(\text{O})-$, wherein q is 1 to 8, and
- (15) $-\text{HN}-\text{CH}_2\text{CH}_2-(\text{OCH}_2\text{CH}_2\text{O})_r-\text{CH}_2-\text{C}(\text{O})-$, wherein r is 1 to 8;

A_2 is an amino acyl residue selected from:

- (1) alanyl,
- (2) asparaginylyl,
- (3) aspartyl,
- (4) glutaminylyl,
- (5) glutamyl,
- (6) leucyl,
- (7) methionyl,
- (8) phenylalanyl,
- (9) prolyl,
- (10) seryl,
- (11) $-\text{HN}-(\text{CH}_2)_q-\text{C}(\text{O})-$, wherein q is 1 to 8,
- (12) $-\text{HN}-\text{CH}_2\text{CH}_2-(\text{OCH}_2\text{CH}_2\text{O})_r-\text{CH}_2-\text{C}(\text{O})-$, wherein r is 1 to 8, and
- (13) glycyl;

A_3 is an amino acyl residue selected from:

- (1) alanyl,
- (2) asparaginylyl,
- (3) citrullyl,
- (4) cyclohexylalanyl,
- (5) cyclohexylglycyl,
- (6) glutaminylyl,
- (7) glutamyl,
- (8) glycyl,
- (9) isoleucyl,
- (10) leucyl,
- (11) methionyl,
- (12) norvalyl,
- (13) phenylalanyl,
- (14) seryl,
- (15) *t*-butylglycyl,
- (16) threonyl,
- (17) valyl,

(18) penicillaminy, and

(19) cystyl;

A₄ is an amino acyl residue of L or D configuration selected from:

- (1) allo-isoleucyl,
- (2) glycyl,
- (3) isoleucyl,
- (4) prolyl,
- (5) dehydroleucyl,
- (6) D-alanyl,
- (7) D-3-(naphth-1-yl)alanyl,
- (8) D-3-(naphth-2-yl)alanyl,
- (9) D-(3-pyridyl)-alanyl,
- (10) D-2-aminobutyryl,
- (11) D-allo-isoleucyl,
- (12) D-allo-threonyl,
- (13) D-allylglycyl,
- (14) D-asparaginy, and
- (15) D-aspartyl,
- (16) D-benzothienyl,
- (17) D-3-(4,4'-biphenyl)alanyl,
- (18) D-chlorophenylalanyl,
- (19) D-3-(3-trifluoromethylphenyl)alanyl,
- (20) D-3-(3-cyanophenyl)alanyl,
- (21) D-3-(3,4-difluorophenyl)alanyl,
- (22) D-citrullyl,
- (23) D-cyclohexylalanyl,
- (24) D-cyclohexylglycyl,
- (25) D-cystyl,
- (26) D-cystyl(*S*-*t*-butyl),
- (27) D-glutaminy, and
- (28) D-glutamyl,
- (29) D-histidyl,
- (30) D-homoisoleucyl,
- (31) D-homophenylalanyl,

- (32) D-homoseryl,
- (33) D-isoleucyl,
- (34) D-leucyl,
- (35) D-lysyl(N-epsilon-nicotinyl),
- (36) D-lysyl,
- (37) D-methionyl,
- (38) D-neopentylglycyl,
- (39) D-norleucyl,
- (40) D-norvalyl,
- (41) D-ornithyl,
- (42) D-penicillaminyl,
- (43) D-penicillaminyl(acetamidomethyl),
- (44) D-penicillaminyl(*S*-benzyl),
- (45) D-phenylalanyl,
- (46) D-3-(4-aminophenyl)alanyl,
- (47) D-3-(4-methylphenyl)alanyl,
- (48) D-3-(4-nitrophenyl)alanyl,
- (49) D-3-(3,4-dimethoxyphenyl)alanyl,
- (50) D-3-(3,4,5-trifluorophenyl)alanyl,
- (51) D-prolyl,
- (52) D-seryl,
- (53) D-seryl(*O*-benzyl),
- (54) D-*t*-butylglycyl,
- (55) D-thienylalanyl,
- (56) D-threonyl,
- (57) D-threonyl(*O*-benzyl),
- (58) D-tryptyl,
- (59) D-tyrosyl(*O*-benzyl),
- (60) D-tyrosyl(*O*-ethyl),
- (61) D-tyrosyl, and
- (62) D-valyl;

A₅ is an amino acyl residue of L or D configuration selected from:

- (1) alanyl,
- (2) (3-pyridyl)alanyl,

- (3) 3-(naphth-1-yl)alanyl,
- (4) 3-(naphth-2-yl)alanyl,
- (5) allo-threonyl,
- (6) allylglycyl,
- (7) glutaminyl,
- (8) glycyl,
- (9) histidyl,
- (10) homoseryl,
- (11) isoleucyl,
- (12) lysyl(N-epsilon-acetyl),
- (13) methionyl,
- (14) norvalyl,
- (15) octylglycyl,
- (16) ornithyl,
- (17) 3-(4-hydroxymethylphenyl)alanyl,
- (18) prolyl,
- (19) seryl,
- (20) threonyl,
- (21) tryptyl,
- (22) tyrosyl,
- (23) D-allo-threonyl,
- (24) D-homoseryl,
- (25) D-seryl,
- (26) D-threonyl,
- (27) penicillaminyl, and
- (28) cystyl;

A₆ is an amino acyl residue of L or D configuration selected from:

- (1) alanyl,
- (2) 3-(naphth-1-yl)alanyl,
- (3) 3-(naphth-2-yl)alanyl,
- (4) (3-pyridyl)alanyl,
- (5) 2-aminobutyryl,
- (6) allylglycyl,
- (7) arginyl,

- (8) asparaginyI,
- (9) aspartyl,
- (10) citrullyl,
- (11) cyclohexylalanyl,
- (12) glutaminyI,
- (13) glutamyl,
- (14) glycyl,
- (15) histidyl,
- (16) homoalanyl,
- (17) homoleucyl,
- (18) homoseryl,
- (19) isoleucyl,
- (20) leucyl,
- (21) lysyl(N-epsilon-acetyl),
- (22) lysyl(N-epsilon-isopropyl),
- (23) methionyl(sulfone),
- (24) methionyl(sulfoxide),
- (25) methionyl,
- (26) norleucyl,
- (27) norvalyl,
- (28) octylglycyl,
- (29) phenylalanyl,
- (30) 3-(4-carboxyamidophenyl)alanyl,
- (31) propargylglycyl,
- (32) seryl,
- (33) threonyl,
- (34) tryptyl,
- (35) tyrosyl,
- (36) valyl,
- (37) D-3-(naphth-1-yl)alanyl,
- (38) D-3-(naphth-2-yl)alanyl,
- (39) D-glutaminyI,
- (40) D-homoseryl,
- (41) D-leucyl,